ABSTRACT OF THE DISCLOSURE

The present invention relates to a method of producing an ungulate having both copies of the IgM heavy chain (mu) rag-1 and/or rag-2 gene eliminated from its genome. Animals which have IgM, rag-1 and/or rag-2 eliminated from their genome are unable to conduct the gene rearrangements that are necessary to generate the antigen receptors of B or T lymphocytes, and therefore will not develop native B or T cells. Because they are unable to produce B and T lymphocytes, these IgM, rag-1 or rag-2 ungulates cannot reject human hematopoietic stem cell preparations, and B and T lymphocytes which develop therefrom. Therefore, the present invention also involves injecting into IgM, rag-1 and/or rag-2 deficient ungulates, in utero or shortly after birth, human B and T lymphocytes whose immune systems produce human immunoglobulin that can be processed for therapeutic uses in humans.

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